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16. Hamilton M. Development of a rating scale for primary depressive illness. *Br J Soc Clin Psychol*. 1967;6(4):278-296.

17. First M, Spitzer RL, Gibbon M, Williams JBW. *Structured Clinical Interview for* DSM-IV-TR *Axis I Disorders, Research Version, Clinical Trials Version (SCID-CT)*. New York: Biometrics Research, New York State Psychiatric Institute; 2002.

18. First M, Gibbon M, Spitzer RL, Williams JBW, Benjamin LS. *Structured Clinical Interview for* DSM-IV *Axis II Personality Disorders (SCID-II)*. Washington, DC: American Psychiatric Press; 1997.

19. Markowitz JC. What is supportive psychotherapy? *Focus*. 2014;12(3):285-289. doi:10.1176/appi.focus.12.3.285

20. Markowitz JC. Interpersonal psychotherapy for chronic depression. *J Clin Psychol*. 2003;59(8):847-858.

21. Rush AJ, Gullion CM, Basco MR, Jarrett RB, Trivedi MH. The Inventory of Depressive Symptomatology (IDS): psychometric properties. *Psychol Med*. 1996;26(3):477-486.

22. Endicott J, Spitzer RL, Fleiss JL, Cohen J. The Global Assessment Scale: a procedure for measuring overall severity of psychiatric disturbance. *Arch Gen Psychiatry*. 1976;33(6):766-771.

23. Ware J Jr, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care*. 1996;34(3):220-233.

24. Hunt SM, McKenna SP. The QLDS: a scale for the measurement of quality of life in depression. *Health Policy*. 1992;22(3):307-319.

25. Bernstein DP, Stein JA, Newcomb MD, et al. Development and validation of a brief screening version of the Childhood Trauma Questionnaire. *Child Abuse Negl*. 2003;27(2):169-190.

26. McHugh RK, Whitton SW, Peckham AD, Welge JA, Otto MW. Patient preference for psychological vs pharmacologic treatment of psychiatric disorders: a meta-analytic review. *J Clin Psychiatry*. 2013;74(6):595-602.

27. National Institute for Health and Care Excellence. Depression in adults: recognition and management. https://www.nice.org.uk/guidance/CG90. Updated April 2016. Accessed June 14, 2016.

Invited Commentary

The Need for Research on Treatments of Chronic Depression

Pim Cuijpers, PhD; Marcus J. H. Huibers, PhD; Toshi A. Furukawa, PhD, MD

Chronic depression is one of the most challenging types of the major depressive disorders to treat, as many patients with chronic depression are resistant to several treatments, leaving clinicians with no or few treatment options available. From a public health perspective, chronic depressive disorders are also problematic because they are responsible for a considerable part of the disease burden of depression. The development of effective treatments for chronic depression is therefore one of the most important challenges for clinical research in depression.

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From this perspective, it is remarkable that only a small number of randomized trials have examined the effects of treatments of chronic depression. Although more than 500 randomized trials have examined the effects of psychotherapies for depression in adults, in a meta-analysis of trials of psychotherapies for chronic depression, only 16 trials were included, 7 of which were in patients with dysthymia.[1] Among the hundreds of randomized trials on selective serotonin reuptake inhibitors and tricyclic antidepressants for depression, a recent meta-analysis found only 20 trials on chronic depression, 19 of which were in patients with dysthymia.[2] A meta-analysis on combined treatments for depression, which is recommended in most treatment guidelines, included only 8 trials.[3] Considering the clinical and public health importance of chronic depression, research on this topic is needed.

The study by Schramm and colleagues[4] in this issue of *JAMA Psychiatry* comparing the Cognitive Behavioral Analysis System of Psychotherapy (CBASP) with supportive therapy (SP) is therefore a welcome addition to the existing research on therapy for chronic depression. Several important research questions are addressed in this trial. One is whether a therapy that has been specifically developed for the treatment of chronic depression (CBASP) should be preferred instead of a nonspecific yet credible psychotherapy (SP). The CBASP is the only therapy that has been specifically developed for the treatment of chronic depression, and it seems safe to assume that this treatment is beneficial to patients, as it is found to result in good rates of response and remission, and superior effects compared with bona fide, nondirective SP.[4] An additional particular strength of the study by Schramm et al[4] is that it allowed enough length and density of treatment for psychotherapy to demonstrate an effect in the acute phase and show growing effects during almost 1 year of treatment.

Like other studies, however, the study by Schramm et al[4] also leaves many important questions unanswered. Most treatment guidelines recommend a combination of pharmacotherapy and psychotherapy for treatment of chronic depression, but it is not clear which psychotherapy should be given. The CBASP would certainly be a good candidate. However, the study by Schramm and colleagues[4] was focused on monotherapy without concomitant pharmacotherapy in patients who mostly preferred psychotherapy. How CBASP, either alone or in combination, would fare in populations that preferred pharmacotherapy or combination therapy or had no preference is still not clear. Nor is the clinically more relevant question of which psychotherapy or combination would be preferable for which patients.

A considerable number of head-to-head comparisons between different types of psychotherapy have shown that the effects of these different types are comparable with each other, with no or only small and nonsignificant differences.[5] Supportive therapy is an exception, with several studies showing that it is somewhat less effective than other therapies. However, this finding may be associated with the fact that SP is often used as a control condition, and may be owing to researcher allegiance, the conviction held by a researcher that a specific treatment is superior to other treatments.[6] Although CBASP is probably effective and somewhat more effective than

SP, it is still not clear whether CBASP is more effective than therapies that were not specifically designed for chronic depression, such as cognitive behavioral therapy and interpersonal therapy. Both cognitive behavioral therapy and interpersonal therapy have also been found to be effective in the treatment of chronic depression,[1] so whether CBASP is superior to these therapies has yet to be established.

Patients in both groups in the study by Schramm and colleagues[4] showed a considerable improvement in depressive symptoms, and the numbers needed to treat for CBASP compared with SP were 5 and 6, respectively, for response and 3 and 7, respectively, for remission. These are not large differences, but are still remarkable in this population of patients with treatment-refractory chronic depression. Medicine, psychiatric or nonpsychiatric, can only rarely work miracles and the median efficacy of standard drug therapies, both in medicine and psychiatry, hover around effect sizes of 0.3 and 0.4.[7] The efficacy of around 0.3 in effect size of CBASP compared with nonspecific bona fide psychotherapy would represent an addition to the armamentarium in psychiatry as great as, or as small as, many other advances in medicine.

Perhaps the most important result of this study is that it confirms what has been found in earlier, smaller trials; namely, that patients with chronic depression can improve. The response rates are overall somewhat lower than in patients with nonchronic depressive disorders after treatment with pharmacotherapy or with psychotherapy, but not very much. That is encouraging news for patients and clinicians.

ARTICLE INFORMATION

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REFERENCES

1. Cuijpers P, van Straten A, Schuurmans J, van Oppen P, Hollon SD, Andersson G. Psychotherapy for chronic major depression and dysthymia: a meta-analysis. *Clin Psychol Rev*. 2010;30(1):51-62.

2. von Wolff A, Hölzel LP, Westphal A, Härter M, Kriston L. Selective serotonin reuptake inhibitors and tricyclic antidepressants in the acute treatment of chronic depression and dysthymia: a systematic review and meta-analysis. *J Affect Disord*. 2013;144(1-2):7-15.

3. von Wolff A, Hölzel LP, Westphal A, Härter M, Kriston L. Combination of pharmacotherapy and psychotherapy in the treatment of chronic depression: a systematic review and meta-analysis. *BMC Psychiatry*. 2012;12:61.

4. Schramm E, Kriston L, Zobel I, et al. Effect of disorder-specific vs nonspecific psychotherapy for chronic depression: a randomized clinical trial [published online February 1, 2017]. *JAMA Psychiatry*. doi:10.1001/jamapsychiatry.2016.3880

5. Barth J, Munder T, Gerger H, et al. Comparative efficacy of seven psychotherapeutic interventions for patients with depression: a network meta-analysis. *PLoS Med*. 2013;10(5):e1001454.

6. Cuijpers P, Driessen E, Hollon SD, van Oppen P, Barth J, Andersson G. The efficacy of non-directive supportive therapy for adult depression: a meta-analysis. *Clin Psychol Rev*. 2012;32(4):280-291.

7. Leucht S, Hierl S, Kissling W, Dold M, Davis JM. Putting the efficacy of psychiatric and general medicine medication into perspective: review of meta-analyses. *Br J Psychiatry*. 2012;200(2):97-106.